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Approved for use through 09/30/2000. OMB 0651-0038  
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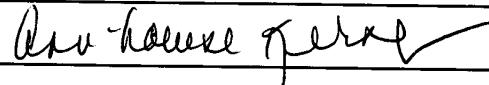
(to be used for all correspondence after initial filing)

|  |   |                        |                |
|--|---|------------------------|----------------|
|  |   | Application Number     | 09/283,431     |
|  |   | Filing Date            | April 1, 1999  |
|  |   | First Named Inventor   | Zhou, et al.   |
|  |   | Group Art Unit         | 1635           |
|  |   | Examiner Name          | K. Lacourciere |
| Total Number of Pages in This Submission | 9 | Attorney Docket Number | 47508.423      |

### ENCLOSURES (check all that apply)

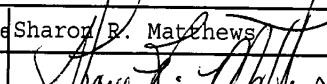
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| <input type="checkbox"/> Fee Transmittal Form                                | <input type="checkbox"/> Assignment Papers (for an Application)                         | <input type="checkbox"/> After Allowance Communication to Group                            |
| <input type="checkbox"/> Fee Attached  | <input type="checkbox"/> Drawing(s)   | <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences        |
| <input checked="" type="checkbox"/> Amendment / Response                     | <input type="checkbox"/> Licensing-related Papers                                       | <input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) |
| <input type="checkbox"/> After Final   | <input type="checkbox"/> Petition Routing Slip (PTO/SB/69) and Accompanying Petition    | <input type="checkbox"/> Proprietary Information   |
| <input type="checkbox"/> Affidavits/declaration(s)                           | <input type="checkbox"/> Petition to Convert to a Provisional Application               | <input type="checkbox"/> Status Letter   |
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| <input type="checkbox"/> Certified Copy of Priority Document(s)              | <input type="checkbox"/> Request for Refund   |  |
| <input type="checkbox"/> Response to Missing Parts/ Incomplete Application   |   |  |
| <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53 |   |  |
| Remarks  |   |  |

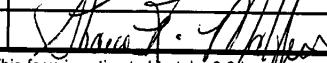
### SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

|                         |   |
|-------------------------|---|
| Firm or Individual name | Ann-Louise Kerner, Ph.D., Reg. No. 33,523   |
| Signature               |  |
| Date                    | July 19, 2001   |

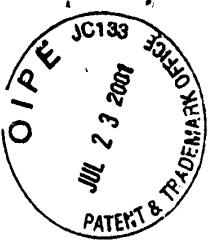
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
(Docket No. 47508.423)

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In re Application of: Zhou, et al. ) Group Art Unit: 1635  
Serial No.: 09/283,431 ) Examiner: K. Lacourciere  
Filing Date: April 1, 1999 )  
Title: MIXED BACKBONE OLIGONUCLEOTIDES CONTAINING  
POPS BLOCKS TO OBTAIN REDUCED PHOSPHOROTHIOATE  
CONTENT

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CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

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Date: 7/19/01

By: Sharon R. Matthews  
Sharon R. Matthews

\*\*\*\*\*  
Commissioner for Patents  
Washington, DC 20231

\*\*\*\*\*  
AMENDMENT AND RESPONSE UNDER 37 C.F.R. §1.111

Dear Sir:

In response to the Office Action dated April 20, 2001, please amend the above-referenced patent application as follows:

In the claims:

*SUB B1*

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4. (Amended) A hybrid oligonucleotide consisting of one or more deoxyribonucleotide POPS blocks and one or more regions of 2'-O-substituted ribonucleotides,